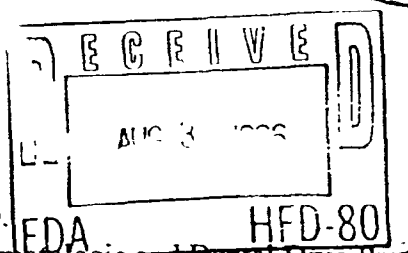
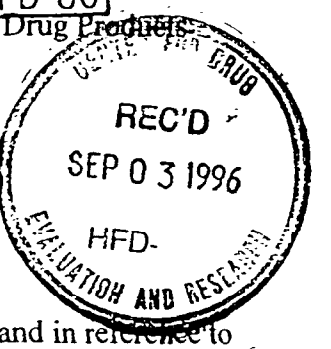
August 30, 1996

ORIGINAL NDA SUBMISSION

Food & Drug Administration
Center for Drug Evaluation and Research
Documents and Records Section
12420 Parklawn Drive
Rockville, MD 20852



Attention: Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
(HFD-540)



RE: Original NDA Submission ~~#20-642~~ 50-744
Periostat™ (doxycycline hyclate capsules USP)

Dear Dr. Wilkin:

Pursuant to Section 505 of the Federal Food, Drug and Cosmetic Act and in reference to 21 CFR 314, we submit in duplicate, this original New Drug Application ~~#20-642 for~~ Periostat™ (doxycycline hyclate, USP) 20 mg Capsules which is proposed for use as part of a professional oral health program to promote periodontal attachment level gain and reduce bone loss, pocket depth and bleeding on probing in patients with adult periodontal disease. Periostat™ acts as an inhibitor of collagenase and, at the proposed 20 mg b.i.d. dose, is not an antibiotic.

Reference is made to our presubmission of the Chemistry, Manufacturing and Controls Section of this NDA on May 30, 1996. A copy of the acknowledgment letter is included as Attachment 1.

As requested by Mr. Frank Cross of the Division, we have provided under separate cover an additional six copies of the Index and Summary sections of this application (Volumes 2.1 and 2.2) and one additional copy of the Clinical Data Summary (Vol 2.20), Integrated Summary of Efficacy text and tables (Vol. 2.21, 2.22), Integrated Summary of Safety text (Vol. 2.34).

CollaGenex Pharmaceuticals, Inc., 301 South State Street, Newtown, PA 18940 USA
215-579-7388 voice 215-579-8577 fax

This application has been the topic for discussion of a Pre-NDA Meeting previously held between CollaGenex and the Division of Medical Imaging, Surgical and Dental Drug Products on May 15, 1995. A subsequent meeting was held on December 21, 1995 with the Division to discuss the toxicology section of this application. All agreements made at these meetings and in subsequent communications have been included in this NDA.

Attachment 2 to the Clinical and Archive copy of this letter are disks containing the WordPerfect® files for the text portions of the final study reports (Studies 5732.11 E, 5732.11F, and 5732.11G) as well as the proposed labeling in Word Perfect 6.1 format.

Attachment 3 to the Statistical and Archive copy of this letter is a disk containing the SAS data sets for Studies 5732.11E, 5732.11F, and 5732.11G. A copy of the accompanying documentation is attached to all copies of this letter.

Please be advised that material and data contained in this submission are confidential. The legal protection of such confidential material is hereby claimed under applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331(J).

If there are any questions concerning this application, please contact the undersigned at 215-579-7619 (telephone) or 215-579-8577 (fax).

Yours truly,

Christopher Powala

Christopher Powala
Director, Drug Development
& Regulatory Affairs

cc: Mr. Frank Cross, Jr., MA, LCDR
Volume 2.1 & 2.2 (6 copies)
Volume 2.20 (1 copy)
Volume 2.21 & 2.22 (1 copy)
Volume 2.34 (1 copy)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date: March 31, 1990.
See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATE FILED
30 Aug 96	
DIVISION ASSIGNED	**NDA/ANDA NO ASS**
540	20642

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314)*.

NAME OF APPLICANT
CollaGenex Pharmaceuticals, Inc.

DATE OF SUBMISSION
August 30,1996

ADDRESS *(Number, Street, City, State and Zip Code)*
301 South State Street
Newtown, PA 18940

TELEPHONE NO *(Include Area Code)*
(215) 579-7619

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER *(If previously issued)*
20-642

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*	PROPRIETARY NAME *(If any)*
doxycycline hyclate capsules USP	**Periostat™**

CODE NAME *(If any)*	CHEMICAL NAME
	4-(Dimethlamino)-1,4,4a,5,5a,6,11,12a-ocatahydo-3,5,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide monohydrochloride

DOSAGE FORM	ROUTE OF ADMINISTRATION	STRENGTH(S)
capsule	**oral**	**20mg**

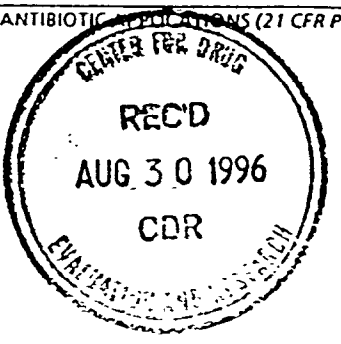
PROPOSED INDICATIONS FOR USE

Treatment of adult periodontitis

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21CFR 314.420)* REFERRED TO IN THIS APPLICATION:

AADA 62-374
AADA 62-839

See Attachment 1 for Drug Master File References



INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

■ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)* ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG	HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION *(Check one)*

☐ PRESUBMISSION ☐ AN AMENDMENT TO A PENDING APPLICATION ☐ SUPPLEMENTAL APPLICATION
■ ORIGINAL APPLICATION ☐ RESUBMISSION

PROPOSED MARKETING STATUS *(Check one)*

■ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)* ☐ APPLICATION FOR AN OVER-THE-COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION		
This application contains the following items: *(Check all that apply)*		
X	1. Index	**Vol 2.1**
X	2. Summary (21 CFR 314.50 (c))	**Vol 2.2**
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))	**Presubmitted on May 31, 1996**
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)	
X	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))	**Vols 2.3-2.4**
	c. Labeling (21 CFR 314.50 (e) (2) (ii))	
X	i. draft labeling *(4 copies)*	**Vol 2.4**
	ii. final printed labeling (12 copies)	
X	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))	**Vols 2.5-2.10**
X	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))	**Vols 2.11-2.17**
X	7. Microbiology section (21 CFR 314.50 (d) (4))	**Vols 2.18-2.19**
X	8. Clinical data section (21 CFR 314.50 (d) (5))	**Vols 2.20-2.109**
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))	
X	10. Statistical section (21 CFR 314.50 (d) (6))	**Vols 2.110, 2.21-2.109**
X	11. Case report tabulations (21 CFR 314.50 (f) (1))	**Vols 2.111-2.128**
X	12. Case reports forms (21 CFR 314.50 (f) (1))	**Vols 2.129**
X	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))	**Vol 2.1**
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))	
X	15. OTHER *(Specify)*	**Vol 2.1**

I agree to update this application with new safety information about the drug that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211.
2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the controlled substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
Christopher V. Powala **Director, Drug Development & Regulatory Affairs**	Christopher V. Powala	8/30/96
ADDRESS *(Street, City, State, Zip Code)*		TELEPHONE NO. *(Include Area Code)*
CollaGenex Pharmaceuticals, Inc. **301 S. State Street, Newtown, PA 18940**		**(215) 579-7619**

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)